Assignment 4: Risk Factors for Progression of Dementia

In this report, a longitudinal study of MRI results of patients both with and without dementia was used to analyze how this disease differs across different groups of individuals as well as over time. More specifically, identifying certain risk factors or warnings for early onset dementia may be beneficial for timely intervention.

The dataset for this analysis, titled "INF2178_A4_data.xlsx" contains 15 columns and 294 rows, where every 2 rows contain test results for one individual over two different points of time. The dataset also contains demographic information such as gender, age, handedness, years of education and socioeconomic status. It is noted that not all individuals completed both rounds of testing. Additionally, it is noted that individuals also change in their group classification between the first and second time of testing.

GROUP	MR1	MR2
CONVERTED	14	12
DEMENTED	64	62
NONDEMENTED	72	70

Table 1: Count of subjects by group classification during first and second visit.

This study contains different tests, the first being measurements taken from the MRI scan to determine intracranial volume which is smaller for patients with dementia. The plot between the first and second visit do show differences in brain volume however it seems quite minimal with no distinct shift towards lower values.

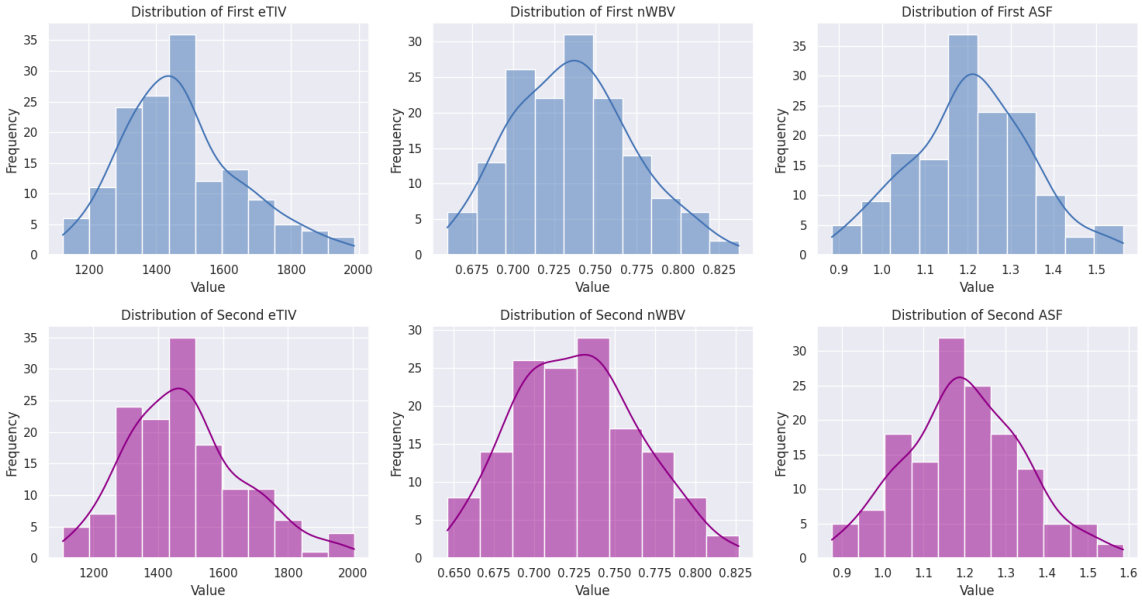

Figure 1: Distribution of MRI tests for brain volume for all subjects during first (top) and second (bottom) visit.

In addition, clinical tests are often used for diagnosing dementia. The Mini Mental State Examination (MMSE) is a questionnaire that computes a score, where a lower number indicates more severe cognitive impairment (where 25+ is considered normal). The plot shows the distribution of subjects and their MMSE scores during the first (left) and second (middle) visit. While there seem to be some differences between the two distributions, it is not clear what the patten is or whether the difference is statistically significant. Lastly, the Clinical Dementia Rating (CDR) assigns a number corresponding to a fixed scale where a higher number indicates more severe dementia. The plot on the right shows that subjects were assigned higher ratings in the second visit.

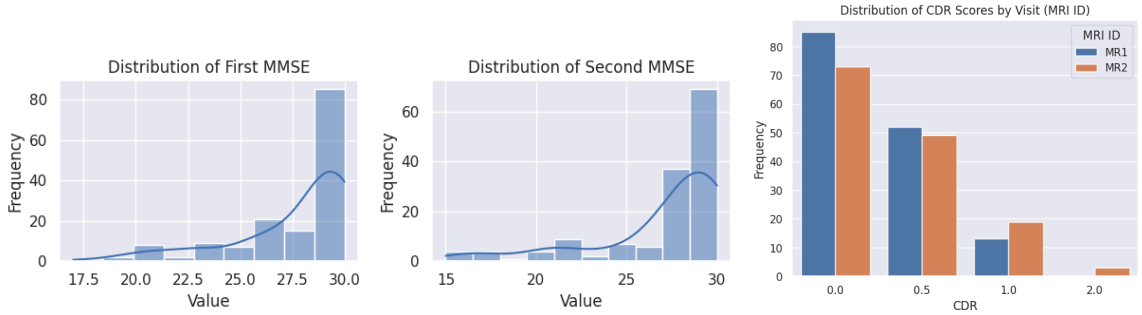

Figure 2: Distribution of MMSE Scores of subjects during the first and second visit (first two plots) and CDR Ratings (right).

From this exploratory data analysis, our research questions include:

1) How do MMSE scores differ between individuals of different socioeconomic status (SES) as well as within individuals over different periods of time?
2) How does intracranial brain volume (as measured by eTIV) differ between individuals of different groups as well as within individuals over different periods of time?

Question 1

A point plot of the MMSE scores across each level of SES shows that the scores are generally lower during the second visit compared to the first. The exception to this is at SES level 2.0 where the scores are similar within both visits. Note that the SES is often ranked from 1 (poor) to 5 (wealthy). The boxplot shows that as we move across each level of SES, the scores decrease (indicating higher cognitive impairment).

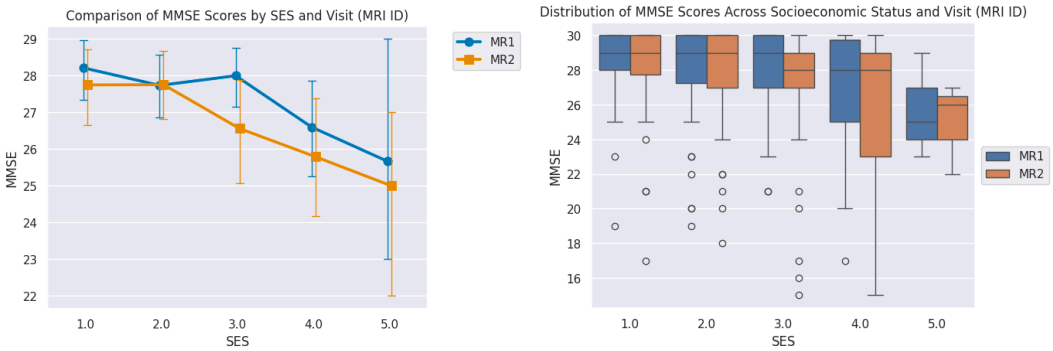

Figure 3: Point plot (left) and boxplot (right) of MMSE scores by SES and Visit.

The summary statistics similarly shows that the average MMSE scores are higher during the first visit and also in lower levels of SES.

MRI ID	**MR1**					**MR2**				
SES	**1.0**	**2.0**	**3.0**	**4.0**	**5.0**	**1.0**	**2.0**	**3.0**	**4.0**	**5.0**
MEAN	28.212	27.738	28.000	26.600	25.667	27.750	27.756	26.562	25.793	25.000
STD	2.472	3.013	2.535	3.729	3.055	3.152	3.121	4.150	4.799	2.646

Table 2: Summary statistics of MMSE scores grouped by level of SES and visit (MRI ID).

To answer our question, a mixed-ANOVA was computed to determine whether MMSE scores differ across SES and MRI ID (with the null hypothesis being that there is no statistical difference) based on a significance level of $\alpha = 0.05$. The results showed that only MRI ID had a p-value less than 0.05, suggesting that MMSE scores differ within subjects during the 2 visits. MMSE may not differ across levels of SES, nor is there a significant interaction between SES and MRI ID for MMSE scores. Post-hoc testing was used to further analyze the relationship between MMSE scores and the two factors,

as pairwise comparison may be able to detect a significant effect between a pair of factors at a specific level even if there is no overall effect. Since there are only two 'levels' to MRI ID, we can a significant result in the mixed-ANOVA suggests that each of the two levels are statistically significant from each other. This is indeed confirmed in the pairwise comparison. However, the results also showed a significant interaction effect between MR1 and SES levels 1.0 and 4.0, suggesting that individuals with SES ranking of 1.0 differed significantly from those with a ranking of 4.0 during the first visit. To validate these findings, it must be confirmed that our dataset meets the assumptions for mixed-ANOVA:

1) Test of Sphericity: the result of 1.0 suggests that the variances of the differences between all possible pairs of related groups are equal. This assumption has been met.
2) Test of Normality: the test for MRI ID showed a result of less than 0.05 for both visits, suggesting that we reject the null hypothesis that the data is normally distributed. The test was repeated for SES, which indicated a non-normal distribution for all levels except for 5.0. Overall, this suggests that the assumption has not been met.
3) Test of Homogeneity of Variances: the test was run separately for each visit (MRI ID), and both resulted in a p-value greater than 0.05. Overall, this assumption has been met.

In conclusion, mixed-ANOVA may not be an appropriate statistical analysis to address our research question due to a non-normal distribution. Central Limit Theorem (CLT) does not apply because the observations between visits are taken from the same subject, hence the samples are not independent. An alternative, non-parametric test may be more appropriate.

Question 2

A point plot of the eTIV across each level of group shows that brain volume is quite similar within both visits, although it tends to be larger in the second visit. The boxplot shows that eTIV is also quite similar across all three groups, although brain volume seems to be largest for "Nondemented" subjects. The plot also shows that within patients with and without dementia, the range is larger and there are more individuals with exceptionally high eTIV (i.e., outliers). This is compared to the "Converted" group, for which the range is much smaller and there do not seem to be any visible outliers.

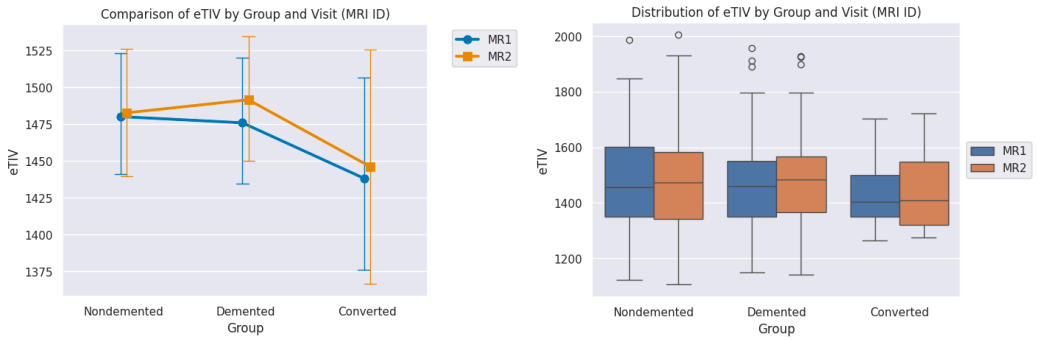

Figure 4: Point plot (left) and boxplot (right) of eTIV by Group and Visit.

The summary statistics shows that the average eTIV is quite similar across all three groups as well as within both visits.

MRI ID	MR1			MR2		
GROUP	**Converted**	**Demented**	**Nondemented**	**Converted**	**Demented**	**Nondemented**
MEAN	1438.286	1475.938	1480.111	1446.250	1491.548	1482.686
STD	132.945	173.615	183.747	150.286	177.258	186.320

Table 3: Summary statistics of eTIV grouped by level of group and visit (MRI ID).

To answer our question, a mixed-ANOVA was computed to determine whether eTIV differs across group and MRI ID (with the null hypothesis being that there is no statistical difference) based on a significance level of $\alpha = 0.05$. The results showed that only MRI ID had a p-value less than 0.05, suggesting that subjects' brain volume changed within the period of the first and second visit. Furthermore, eTIV does not differ across each level of group, nor is there an interaction between group and MRI ID on brain volume. Post-hoc testing was used to further analyze the relationship between eTIV and the two factors. The results confirmed that eTIV significantly differs within MRI ID (where the p-value is less than 0.05), but not across groups. To validate these findings, it must be confirmed that our dataset meets the assumptions for mixed-ANOVA:

1) Test of Sphericity: the result of 1.0 suggests that the variances of the differences between all possible pairs of related groups are equal. This assumption has been met.
2) Test of Normality: the test for MRI ID showed a result of less than 0.05 for both visits, suggesting that we reject the null hypothesis that the data is normally distributed. The test was repeated for the group factor; the results also showed that the data is not normally distributed across all levels. Overall, this suggests that the assumption has not been met.
3) Test of Homogeneity of Variances: the test was run separately for each visit (MRI ID), and both resulted in a p-value greater than 0.05. Overall, this assumption has been met.

In conclusion, mixed-ANOVA may not be an appropriate statistical analysis to address our research question due to a non-normal distribution. Central Limit Theorem (CLT) does not apply because MRI ID and Group are not independent variables. An alternative, non-parametric test may be more appropriate.

Statistical Power Analysis

Given a theoretical experiment with an effect size of 0.7, alpha level of 0.5, and power of 0.91, a minimum sample size is 46 subjects. The plot below demonstrates how statistical power dramatically increases as sample size increases up until around 40 participants. As the power approaches 1.0, the curve begins to flatten.

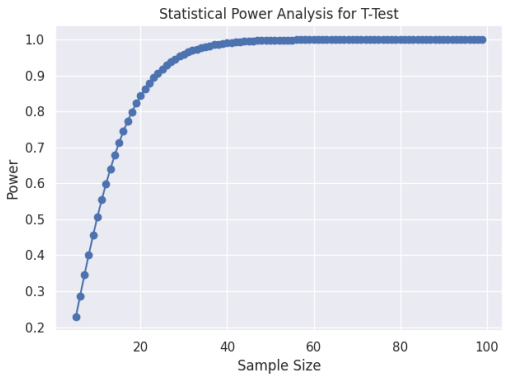

Figure 5: Sample Power Curve for T-Test.